
Genome-Wide Binding Map of the HIV-1 Tat Protein to the Human Genome.

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Public Summary:

This work utilized some of the computational methods we had developed for our stem cell studies to examine how a protein encoded by the Human Immunodeficiency Virus (HIV) interacts with the human genome. We found that the viral protein binds to specific regions of the genome in T lymphocytes, a type of immune cells, to potentially regulate expression of specific genes which function in T cell biology in a way as to favor production of viral progeny.

Scientific Abstract:

The HIV-1 Trans-Activator of Transcription (Tat) protein binds to multiple host cellular factors and greatly enhances the level of transcription of the HIV genome. While Tat's control of viral transcription is well-studied, much less is known about the interaction of Tat with the human genome. Here, we report the genome-wide binding map of Tat to the human genome in Jurkat T cells using chromatin immunoprecipitation combined with next-generation sequencing. Surprisingly, we found that approximately 53% of the Tat target regions are within DNA repeat elements, greater than half of which are Alu sequences. The remaining target regions are located in introns and distal intergenic regions; only approximately 7% of Tat-bound regions are near transcription start sites (TSS) at gene promoters. Interestingly, Tat binds to promoters of genes that, in Jurkat cells, are bound by the ETS1 transcription factor, the CBP histone acetyltransferase and/or are enriched for histone H3 lysine 4 tri-methylation (H3K4me3) and H3K27me3. Tat binding is associated with genes enriched with functions in T cell biology and immune response. Our data reveal that Tat's interaction with the host genome is more extensive than previously thought, with potentially important implications for the viral life cycle.

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